Masland, Richard L.

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HOW IT CAN BE PREVENTED.

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BLINDNESS: WHY IT OCCURS AND HOW IT CAN BE PREVENTED

Richard L. Masland

Americans fear blindness more than any other affliction except cancer, according to a recent Gallup poll. Yet, in spite of research advances, an increasing number of persons fall victim to this affliction each year.

Throughout the world 10 million live without sight. In the United States there are more than 410,000 legally blind persons, and hundreds of thousands more whose visual loss prevents reading newsprint. Each year more than 30,000 lose their sight, and many others have visual handicaps which can be compensated only by artificial means to produce adequate vision.

Whether loss of sight is considered in terms of total blindness, functional blindness, or various degrees of limitation on the ability to see, it is clear that disabilities of the eye constitute a vast problem.

Through recorded history, man has recognized his responsibility to care for the blind and to devise means of helping them compensate for their visual loss. In this country particularly, much attention has been given to the care and rehabilitation of the blind. An increasing amount of aid is available to the blind to help them obtain education and lead an independent, self-sufficient life.

But caring for the blind is not enough in this era of scientific discovery and medical advancement. Wherever possible the tragedy should be prevented. Much of the blindness in this country results from disorders whose cause is unknown to science. The urgent need, therefore, is for medical research to increase the understanding of the visual process and to learn more about the causes of blindness in order to find ways to prevent and treat the disorders. As one of the National Institutes of Health (NIH), the research establishment of the Public Health Service, the National Institute of Neurological Diseases and Blindness (NINDB) conducts and supports research and training to achieve these objectives.

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Aspects of NINDB Programs

Institute programs have three aspects. In its own laboratories at the National Institutes of Health, a small group of scientists use the techniques of chemistry, electron microscopy, histology, and physiology to gain new knowledge of eye disorders. Closely related to these laboratory studies is a ward in the Clinical Center, the NIH hospital facility, where eye patients receive the best possible treatment while being closely observed for information on the results of treatment.

Intramural studies conducted in its own laboratories and clinics at NIH comprise only a small part of the Institute's total effort. At universities and hospital centers throughout the country, laboratory scientists and physicians study eye disorders under NINDB grant support. Some of these studies involve patients; some, laboratory techniques; and others combine a number of different approaches to gain an overall picture of visual mechanisms and of eye diseases.

Finally, in order to assure a continuing supply of men to carry on these research programs, the Institute also supports a number of training programs at universities and other training centers throughout the country. The Institute's expenditures for eye research and training grew from a modest $700,000 in 1954 to $17.4 million in 1967 (Table). Over this period, more than $97 million will have been made available for eye research.

Table
Total Appropriations and Funds Obligated for Vision
National Institute of Neurological Diseases and Blindness
(In thousands)

Year	Total appropriation	Obligations for vision	Non-categorical obligations[1]
1954......	$4,500	$675	$10
1955......	7,601	1,575	169
1956......	9,861	2,115	293
1957......	18,650	3,210	451
1958......	21,387	3,940	1,079
1959......	29,403	5,079	748
1960......	41,487	7,120	1,669
1961......	56,600	8,489	9,632
1962......	70,812	9,925	6,683
1963......	83,506	10,951	10,783
1964......	87,675	12,821	10,631
1965......	87,821	14,342	8,759
1966(Est.).	101,153	16,473	11,885
1967(Est.).	106,418	17,410	13,346

[1] These funds support total Institute efforts, and are not identifiable by disease category. Included are General Research Support Grants, Review and Approval, Program Direction, transfers, and Scientific Evaluation Grants.

Cures for Some Eye Disorders and Greater Understanding of Other Disorders

During the 15 years since the Institute's establishment, its investigators have discovered dramatic cures for a few eye disorders and have greatly broadened their understanding of many others. For example, in 1953 a large cooperative study clearly confirmed the suspicion that too much oxygen was responsible for retrolental fibroplasia (RLF) as a cause of blindness. As a result of changed practices that were undertaken, the incidence of retrolental fibroplasia fell dramatically from 1,900 cases in 1952 to only 28 in 1958. Today RLF is a rarity, although it still occurs among infants of extremely small birth weight who must have oxygen to survive.

The cost of caring for one blind person, at least $1,000 per year, for an average life span of 65 years would total $65,000. Had the cause of RLF been discovered one year later, the lifetime-cost of caring for the additional number of persons who would have become blind during that year would have been $121 million. If the cause had not been discovered for a decade, the cost to the Nation would have been more than $1 billion.

Medical advances of the past 50 years have brought a shift in the relative importance of the various causes of blindness. Infectious diseases and injuries, prominent causes of blindness early in the century, have been brought increasingly under control through new drugs, surgical advances, and public health measures. But in their place, the general diseases (especially diabetes, arteriosclerosis, hypertension, and nephritis), as well as glaucoma and cataract have become increasingly important as major causes of blindness. All of these disorders occur with increasing frequency with advancing years. Cataract, glaucoma, and vascular disorders of the eye account for more than 50 percent of blindness in this country today.

RESEARCH

Intramural Research

During the early life of the Institute's eye research programs, an important new cause of uveitis, an eye disease that particularly afflicts infants, was discovered. Working with scientists in the infectious disease laboratories at NIH and with some of the first patients to be admitted to the Clinical Center, Institute ophthalmologists found that toxoplasmosis was a prominent cause of uveitis. Since that time, much has been learned about this type of infection, both in the eye and in other parts of the body. Several hundred uveitis patients have been admitted to the Clinical Center for close observation and treatment with drugs. A new antibiotic, spiramycin, was found to be effective when used in combination with the usual treatment for uveitis. And folonic acid was found to prevent adverse effects of daraprim, another drug used to treat uveitis.

The Institute's opportunity to correlate basic and clinical research is especially fruitful in such disorders as uveitis, where a number of laboratory tests are required to determine the agent responsible for the inflammation. Clinical studies in ophthalmology were also helpful in demonstrating that blindness could result from large doses of chloroquine, sometimes used to treat rheumatoid arthritis and related disorders. By studying 14 patients who received this drug over a period of several years, investigators were able to devise a simple test to detect retinal changes in the early stages while the damage could still be repaired.

Extramural Research

Research at the Bethesda laboratories is only a small part of the Institute's research effort against blindness. Universities, hospital centers, and public and private research institutions throughout the country receive grants from the Institute to conduct research on blinding disorders. Support is also given for constructing and equipping research facilities and for the maintenance of hospital patient beds. Grant programs are designed to promote the highest quality of independent research by the existing scientific community.

Institute-supported vision research covers a broad range of studies. although cataract, glaucoma, and retinal disorders of vision receive the major share of support, lesser known disorders, such as amblyopia, tumors, strabismus, and infectious diseases of the eye are also studied.

Grantee studies have led to a better understanding and improved treatment of glaucoma. Although this blinding disorder cannot yet be cured, loss of sight can often be prevented by using drugs to lower the intraocular pressure and by avoiding damage to surrounding eye tissues. Even more helpful has been the discovery that glaucoma is inherited as a recessive trait. Offspring, without getting the disease themselves, may still be carriers and pass the disorder on to their children. Means of preventing glaucoma may be years away, but the more immediate goal of control to prevent loss of vision is now possible in most cases.

Chemical research by Institute grantees has provided valuable data on the physical and chemical properties of lens proteins. Since the formation of cataracts is associated with accumulation of insoluble proteins, these data will be valuable in understanding cataracts.

Cataracts at present can be treated only by surgical removal of the opaque lens. Several years ago Institute-supported scientists undertook studies which helped prove the safety and usefulness of alpha chymotrypsin in cataract operations. Animal studies in the laboratories of various research centers proved that the enzyme may be used without harm to the surrounding eye tissues. Since then the enzyme has been widely used in cataract surgery, making the operation one of the most successful in medicine Numerous 90-year-old patients, their sight restored by cataract surgery, have been up and about in a few days.

Herpes simplex virus, a common cause of corneal ulcers and blindness, is an infection which has recently received considerable attention because of the cure discovered by an investigator who was supported by the Institute during various stages of his training. He first joined the Institute as a Clinical Associate at the Clinical Center in Bethesda. Later, as a fellow at the Massachusetts Eye and Ear Infirmary in Boston, he continued his laboratory experiments, extended them to the study of viruses, and produced the first successful drug treatment of a true viral disease in man. Working with animals first, to be sure the treatment was safe and effective, he cured herpes simplex virus with a drug developed to treat cancer. Since that time, the drug iodo-deoxyuridine (IDU) has been used to save the vision of many patients with viral diseases of the cornea.

Some people who were blinded by viral and other diseases of the cornea have, fortunately, had vision restored through half-thickness corneal transplants, in operations in which tissue from donated human eyes replaces the diseased cornea. Institute studies have resulted in improved methods of freezing and dehydrating donor material for long-range storage and shipment.

Corneas must be "alive"--removed within 48 hours after death--to be used successfully in full-thickness transplants. This necessity created a difficult problem in the widespread use of this method of restoring sight to some persons with diseased or scarred corneas. But recently a method of freezing at a precisely controlled rate to minus 190 degrees has kept corneal tissue alive in suspended animation over considerable periods of time. Corneal tissue preserved in this fashion has been found as suitable as fresh tissue and has greatly extended this method of treatment.

The work of a Boston grantee and an Institute fellow offers new hope for some patients for whom corneal transplants are unsuccessful or cannot be used. In their work, reported in 1965, a corneal implant of transparent silicone restored partial vision in 30 patients suffering from one of the most severe corneal diseases, corneal edema.

Since some failures of corneal transplants were recently found to be due to abnormal donor tissue, principally from elderly donors, stains have now been developed to identify changes in transplant material that would make it unsuitable for a corneal transplant operation.

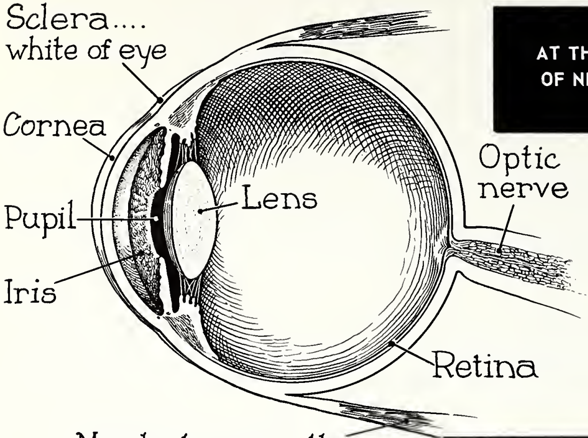
Trachoma, not a large problem in the United States as a whole, is still prevalent among Indians and Mexicans in southwestern States. But in the world at large, trachoma, a chronic disease of the cornea and conjuctiva leading to corneal scarring, is still the leading cause of blindness. It spreads in families and is encouraged by poverty and poor hygiene. The disorder can be cured by drugs, but there is a lack of natural immunity and frequent reinfection is common.

Attempts to eradicate trachoma through mass antibiotic campaigns have been successful only in the more highly developed nations. In other countries such campaigns have either failed to cure or there has been a high percentage of relapsed cases and reinfection. This is true even among Indians in the southwestern United States.

After the trachoma virus was first successfully isolated in 1957, additional years of research produced vaccines with generally favorable results. Research is continuing both to overcome vaccine-induced infections observed in some cases and to develop a relatively easy way to produce a high potency vaccine. The development of the immunofluorescent technique--a means to view under an ultraviolet microscope stained scrapings from the conjunctiva--has been a major breakthrough in the diagnosis of early trachoma.

Millions of Americans are affected by non-blinding visual disorders including refractive errors such as myopia (nearsightedness), hyperopia (far sightedness), astigmatism (defective curvature of the refractive surface), strabismus (crossed eyes) and amblyopia ex anopsia (lazy eye). These conditions result in eye strain, discomfort, fatigue, and inability to see clearly. Their identification and correction are of great importance, particularly in children, where uncorrected defects may seriously interfere with learning.

EYE RESEARCH AT THE NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND BLINDNESS



The applanation tonometer is used to measure intraocular pressure in the diagnosis of glaucoma.

The dissecting microscope is used to cut ultra thin sections of eye tissue for examination under the electron microscope.

Institute grantees are investigating optics and refractive disorders. The use of high speed computers and ultrasound to measure different parts of the eye may lead to greater understanding in these areas.

One of the more prevalent and serious of these disorders ia amblyopia ex anopsia, a form of blindness in one eye due to nonuse. It takes a great toll in learning ability, lack of depth perception for driving and other aspects of daily living. There are two avenues open for its elimination. If the disorder is discovered in early childhood, before school age, the handicap can often be corrected by occluding (covering) one eye for a period, by orthoptic exercises and other means. For this reason, eye physicians are putting more stress on ophthalmological examination of children within the first year or two of life.

However, even with increased alertness for amblyopia in young children, there will continue to be cases which remain undiagnosed until it's too late. to treat them by conventional means.

For this reason, scientists would like a clearer insight into the nature of the processes leading to amblyopia. They believe that significant progress in the treatment of strabismus and amblyopia must await a more thorough understanding of the normal mechanisms of vision, from the absorption of light by the retina to the interpretation of a visual message in the brain. Studies of the eye muscles may also improve treatment of amblyopia. New insight provided by advances in control and systems engineering has stimulated a fresh approach to the study of eye movements and how they affect vision.

Greater knowledge of the function and structure of all parts of the eye is needed. An understanding of the retina is critical to eye research, for it performs the most sophisticated function by acting on light and converting it into electrical impulses that travel to the brain. All other parts of the eye serve the retina; some protecting it, and others directing light to it. Investigators are progressing in their study of the complex structure of the retina.

Studies of the relation of the mechanism of vision to perception of time, space, color, brightness, and form continue to receive support. For more than 150 years it has been known that the retinal cones transmit color impulses. However, recent study reveals that there are three types of cones, each of which is specific for a color: red, green, or blue. The three groups of cones function together to transmit electrical impulses for all primary colors and their shadings. Further study of this system should provide a better understanding of color blindness.

The basic response of retinal cells to light is being investigated. The ERG (electroretinogram) and a related test, the EOG (electrooculogram), both measure the eye's electrical response to stimulation and provide sensitive and accurate measurements of retinal damage. These tests indicate whether the retina is defective and, if so, whether the defect lies in the rods or cones. A defect in either of these photoreceptors will impair vision.

Program-Projects

In addition to supporting research projects related to specific problems of the blinding diseases, the Institute is now developing a group of eye research centers in which strong multidisciplinary teams are being mobilized to carry out a broad-scale attack on these disorders. Excellent studies have been reported from four of these vision program-projects now in full operation: The Retina Foundation in Boston, The Neurosensory Center at the State University of Iowa, the University of Chicago Program-Project for studies on glaucoma and disorders of the retina, and the Research Center for Corneal Disorders at Columbia University in New York. This year, with funds appropriated specifically for this purpose, three new centers have been established at the Massachusetts Eye and Ear Infirmary in Boston, at the Institute of Medical Services in San Francisco, and at the University of California in San Francisco.

Research horizons in the vision field have been widened through the award of grants for eight outpatient vision research units. Thousands of persons with eye disorders not sufficiently debilitating to require their hospitalization can now be seen in the outpatient units on a regular basis by physician-scientists seeking solutions to such problems as uveitis, glaucoma, and other diseases.

Among the advantages offered by the new centers are opportunities to study ocular diseases which affect only human beings and cannot be duplicated in animals, and to continue research which has reached its limits in the laboratory or in animal trials. Specific conditions to be studied include: human macular diseases, or diseases affecting central vision, diseases of the retina; diabetic retinopathy; corneal research; herpetic karatitis, and ocular pharmacology.

Grants totaling $288,000 for FY 1967 have been made to: Jefferson Medical College in Philadelphia; University of Wisconsin at Madison; Duke University in Durham, N.C.; New York University Medical Center; University of Miami School of Medicine; the Wills Eye Hospital Research Institute, Philadelphia; Boston University Hospital; and Mount Sinai Hospital in New York City.

Information and Program Analysis Centers

In 1966, NINDB established a Vision Information Center at Harvard University's Francis A. Countway Library of Medicine in Boston. Within the center, some of the Nation's outstanding scientists will review and analyze the world-wide literature and research reports on eye disorders; establish an information storage and retrieval system; supervise the preparation of abstracts, summaries, reviews and analyses of these data; and make this information available, both to the Institute for program planning and to the scientific community at large.

Training Program

The Institute supports the training of research workers both directly through fellowships and indirectly through grants to medical schools and other institutions. Medical doctors may receive training to become ophthalmologists or to go into some other medical specialty. Scientists may receive support for training during residency or afterwards; basic scientists such as chemists, physiologists, and pharmacologists may apply for support before obtaining a Ph.D. degree or afterwards for further training.

NINDB's research fellowship program assists scientists preparing for careers in research by supporting part of the costs of the necessary academic training and research experience. Research fellows are proving an effective means of maintaining a continuing supply of research manpower.

The postdoctoral fellowship program is also helping to increase the number of individuals trained for research and related teaching in fields concerned with visual disorders. Postdoctoral training may be arranged in any recognized institution within the United States, including governmental research laboratories with appropriate resources, or in a foreign country when the training best suited to the applicant's purpose is available there. Postdoctoral fellowships are awarded for one year with assurance of support for one or two more years if the need is shown.

Scientists have also gained a new understanding of retinitis pigmentosa and other inherited disorders of the retina. Mice, rats, and dogs have been helpful in improving tests which show how well the retina is functioning and identifying defects.

The close resemblance of retinitis pigmentosa to night blindness suggested local abnormality in vitamin-A metabolism. However, administration of vitamin-A supplements that improved night blindness due to a vitamin-A deficiency had no effect on retinitis pigmentosa. Studies revealed basic differences in the early chemical changes in the retina of animals with the two disorders.

The finding that the progress of a retinitis pigmentosa-like disorder in rats could be retarded by keeping them in dim light suggests that humans with retinitis pigmentosa might help protect their eyes by wearing dark glasses. This hypothesis cannot readily be tested, for sight loss in this disorder is so slow and unpredictable that recognition of the beneficial effects of light control or of other therapy is difficult.

By using various approaches, a fuller understanding of the normal process of vision may be obtained. Once the normal function is understood, many of the defects and disorders of the eye may also yield to understanding and treatment.

PROGRAM DEVELOPMENTS

The program of grants available primarily for individual project support has been strengthened and broadened over the years. Grants have been provided for projects for broad-based multidisciplinary attacks on research problems; cooperative studies which pool the research findings of several institutions; conferences for dissemination of data and exchange of ideas; committees or workshops to study a particular problem; and collaborative epidemiological studies such as the Institute-sponsored program for the collection of data on the epidemiology of eye disorders.

Subcommittee on Vision and Its Disorders

A special planning committee was organized in 1965 by NINDB's Advisory Council to provide for total review and planning of program in relation to visual disorders. This committee, composed of Council members and other consultants, is investigating the state of knowledge and identifying areas needing special attention. Under its guidance, the Institute hopes to develop a number of projects to study diagnostic procedures, evaluate treatment, make epidemiological studies, and investigate the "life history" of diseases as they affect patients of different ages.

To obtain special fellowships for special training not available through other fellowship programs, candidates must have had at least three years of relevant research or professional experience, or have completed residency training in a clinical specialty or its equivalent.

Research career development awards are for young investigators, such as associate professors, who need further experience and training to qualify for senior positions in independent research and teaching.

Training grants are awarded to institutions--professional and graduate schools, hospitals and accredited clinics--rather than to individuals. They may include funds for equipment, personnel, and other costs involved in expanding or improving an existing program or in establishing a new one. In some cases, stipends for individuals are awarded by the institution from training grant funds.

In FY 1965, 450 individuals received scientific training through NINDB training programs. These programs have increased the pool of teacher-investigators to perform eye research and to train others as teachers, investigators, and practicing physicians. Some graduate trainees go out and set up their own training programs in medical schools where no ophthalmology residencies existed before. The result has been an increased awareness of eye research across the board, in medical schools, in residencies, and in research and treatment centers.

Improving the Quality of Blindness Statistics

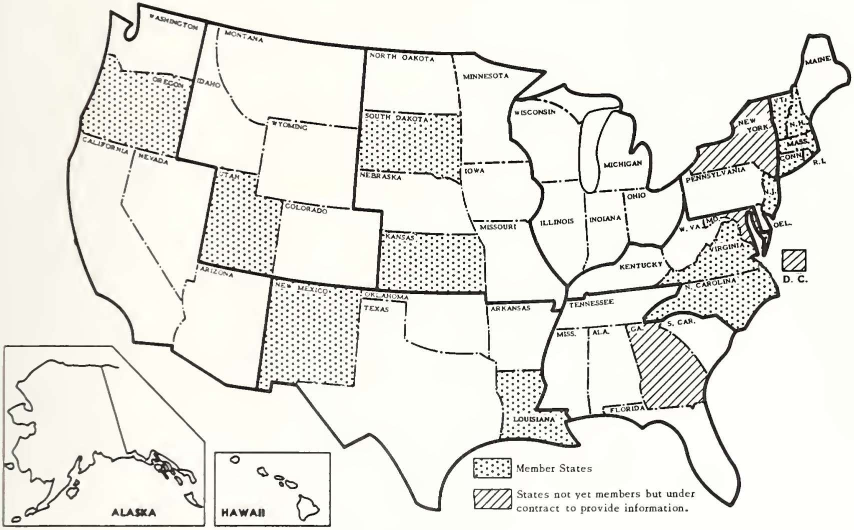
The lack of reliable national statistics on blindness has been a continuing problem. From 1830 through 1930, the Census Bureau recorded data on the number of blind according to age, cause of blindness, age of occurrence, race, sex, and various other demographic and social factors. But accurate information was never obtained, due largely to the problems of definition, personal judgment of census takers, and the tendency of respondents to conceal the presence of blindness in their relatives.

In surveys covering the periods July 1957-June 1961 and July 1963-June 1965, the National Health Survey has focused on the number and severity of visual impairments by age and sex. A "severe visual impairment" is one in which a person is "unable to read ordinary newsprint with glasses" and is accordingly limited in "ability to work, keep house, or go to school." The National Health Survey, conducted by the National Center for Health Statistics in the U.S. Public Health Service, is based on interviews of a minimum of 36,000 households selected to be closely representative of the civilian, noninstitutional population.

To complement the survey method, in gathering data on visual impairments, the National Institute of Neurological Diseases and Blindness is developing a Model Reporting Area for Blindness Statistics. Its purpose is to promote standardized and complete reporting on State blindness registers and to permit more meaningful comparisons and development of statistical aggregates. The Institute, together with the Division of Chronic Diseases in the U.S. Public Health Service, has given assistance and guidance to those States wishing to revise their registers to conform to MRA standards.

MODEL REPORTING AREA FOR BLINDNESS STATISTICS

Federal-State Program under the National Institute for Neurological Diseases and Blindness



Membership in the Model Reporting Area includes 14 States, and four additional States are under contract with NINDB to provide information. The total population of these 18 States represents a third of the population of the United States. As more States join the project, the Institute's yearly compilation of figures from the Registers will reflect the extent of the blindness problem nationally.

FUTURE POTENTIAL OF RESEARCH ON BLINDNESS

As indicated by this brief review of current developments in the study of visual disorders, research is extremely complex, and the causes of blindness are many. The present unsolved problems in the field are legion, but there are many hopeful elements: great strides have been made in research in the last few years; more well-trained investigators are available; more research projects are under way; and there are more well-equipped eye research centers. This does not mean that the needs for manpower, money, and facilities have been met, but progress in the right direction is well under way.

SELECTED REFERENCES

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service, National Institute of Neurological Diseases and Blindness

Cataract and Glaucoma, Hope through Research, PHS 793.
Eye Research, National Institute of Neurological Diseases and Blindness, PHS 1502. 45 p.
Research Grant Support in the Neurological, Sensory and Communicative Fields.
Summary of Progress in Eye Disorders. Research Profile No. 3 PHS 1155, 1965. 17 p.
Training Support in the Neurological, Sensory and Communicative Fields.

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